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Abstract: Background More than 700,000 trips were made by residents in England, Wales, and Northern Ireland (EWNI) to tropical countries endemic for yellow fever, a potentially deadly, yet vaccine-preventable disease transmitted by mosquitoes. The aim of the study was to map and ascertain the geographical accessibility of yellow fever vaccination centres (YFVC) in EWNI.

Methods The location of 3,208 YFVC were geocoded and the average geodetic distance to nearest YFVC was calculated for each population unit. Data on trips abroad and centres were obtained regionally for EWNI and nationally for the World Top20 countries in terms of travel.

Results The mean distance to nearest yellow fever vaccination centre was 2.4km and only 1% of the population had to travel more than 16.1km to their nearest centre. The number of vaccines administered regionally in EWNI was found correlated with the number of trips to yellow fever countries. The number of centres per 100,000 trips was 6.1 in EWNI, which was below United States (12.1) and above the rest of Top20 countries.

Conclusions The geographical accessibility was good and the service availability in line with demand regionally. Variation in service accessibility internationally likely relates to different travel patterns/demand and differences in healthcare systems.



Travel Medicine and Infectious Disease

Conflict of Interest Policy

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Declarations

Travel Medicine and Infectious Disease requires that all authors sign a declaration of conflicting interests. If you have nothing to declare in any of these categories then this should be stated.

Conflict of Interest

A conflicting interest exists when professional judgement concerning a primary interest (such as patient's welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the authors when they have financial interest that may influence their interpretation of their results or those of others. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

Please state any competing interests

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Please state any sources of funding for your research

Signature (a scanned signature is acceptable, but each author must sign)

Print name

Title

Geographical accessibility to yellow fever travel vaccination centres in England, Wales, and Northern Ireland

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Abstract (200/200 words)

Background More than 700,000 trips were made by residents in England, Wales, and Northern Ireland (EWNI) to tropical countries endemic for yellow fever, a potentially deadly, yet vaccine-preventable disease transmitted by mosquitoes. The aim of the study was to map and ascertain the geographical accessibility of yellow fever vaccination centres (YFVC) in EWNI.

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Conclusions The geographical accessibility was good and the service availability in line with demand regionally. Variation in service accessibility internationally likely relates to different travel patterns/demand and differences in healthcare systems.

Key words (max 6)

GEOGRAPHICAL ACCESSIBILITY, PREVENTIVE MEDICINE, VACCINATIONS, YELLOW FEVER

1. Introduction

The populations of England, Wales, and Northern Ireland made more than 60 million trips abroad in 2015 [1]. More than 700,000 of these trips were made to countries endemic for yellow fever, a potentially deadly, tropical disease transmitted by mosquitoes. The disease is preventable by vaccination and this study was undertaken to elucidate the geographical accessibility of yellow fever vaccination centres.

Yellow fever control has been on the international public health agenda since 1851 and has remained a disease under tight international surveillance and control measures ever since together with diseases such as cholera, and pneumonic plague [2]. Due to its reservoir in monkey and other non-human primate populations in the rain forests of Africa and South America (the forest cycle is maintained with tree-living mosquitoes as vectors), yellow fever may never be eradicated [3]. The main control measure for yellow fever is therefore vaccination in combination with vector control in high risk areas as well as measures available to countries at risk of importing or exporting the disease such as vaccination certificate requirements, border vaccination, and emergency quarantine restrictions to reduce the international spread of the disease [2,4,5].

Occasionally, there are large outbreaks in urban areas (urban cycle), where the transmission depends on the *Aedes aegypti* mosquito, which has spread in cities across the tropics in recent decades. A yellow fever outbreak in Angola and Democratic of Republic of Congo (DRC) in 2015-2016 with more than 7,000 suspected cases (965 confirmed cases and 137 confirmed deaths) was a stark reminder of the emerging threat of urban yellow fever outbreaks [6,7]. Increased international travel, urbanisation, and the fact that many tropical countries have large unvaccinated populations make the prospects of new urban yellow fever outbreaks a particular concern. At least 42 cases of international spread were recorded in connection with the Angola-DRC outbreak to countries with vector presence and largely unvaccinated populations including China and Kenya [8].

The National Travel Health Network and Centre (NaTHNaC) has overseen the registration, training, clinical standards, and audit of yellow fever vaccination centres in England, Wales, and Northern Ireland in compliance with the International Health Regulations for yellow fever since 2005 [9] and this is the first study to evaluate the geographical accessibility [10] of the yellow fever vaccination services. The aims of the study were thus to map and ascertain the geographical accessibility of yellow fever vaccination centres, match the number of trips to countries with yellow fever risk to the number of vaccinations given per region, identify any underserved

populations and evaluate any need to regulate service provision, and gather data to support contingency planning in the event of a vaccine shortage.

2. Methods

Administrative data on the postcode location of yellow fever vaccination centres were extracted from the Yellow Fever Vaccination Programme database (NaTHNaC, 27 October 2016). Occupational Health departments (N=218) were excluded as these by definition were not open to the general public. A total of 3,222 centres were registered. General practitioner (GP) practices were the most frequent type of centre (N=2,381). Of the 3,222 centres, 3,208 or 99.6% could be geo-located to Census 2011 lower layer super output area (super output area for Northern Ireland; this is the nearest equivalent unit and it will be referred to as lower layer super output area hereinafter) and UK Region using the Office for National Statistics (ONS) Postcode Directory, August 2016 [11]. The latest mid-year population estimates (2015) were obtained at lower layer super output area level from ONS [12] and the Northern Ireland Statistics and Research Agency (NISRA) [13]. The analyses were conducted at lower layer super output area (N=35,643), which had a mean (SD) population of 1,676 (379). The average geodetic distance (crow-fly distance) from each population unit was calculated to each centre location using the Stata module, GEODIST [14] to determine the distance to the nearest centre at lower layer super output area level. The centres were assigned to distance categories according to the following population percentiles: 75th, 90th, 95th, and 99th. Data on the average number of vaccinations per centre across regions were obtained from annual surveys of the centres in 2013-2015 (NaTHNaC, unpublished data). Boundary data for Census output areas, UK Regions and countries were obtained from the UK Data Service/Edinburgh University Data Library [15], which contains National Statistics data (© Crown copyright and database right, 2016), NRS data (© Crown copyright and database right, 2016, Source: NISRA Website, www.nisra.gov.uk; accessed 17 November 2016), and OS data (© Crown copyright and database right, 2016). Boundary data for the Isle of Man, Republic of Ireland, and Scotland were obtained from Natural Earth (www.naturalearthdata.com; accessed 17 November 2016). Maps were created using Quantum GIS 2.12 [16]. Data on trips abroad by UK region of residence undertaken in 2015 were obtained from ONS Social Surveys (Crown copyright; December 2016). Data on trips abroad by countries where the traveller spent most time and UK Region of residence were obtained from Office for National Statistics [1]. Data on countries with risk of yellow fever transmission were obtained from the World Health Organization [17]. Data on the number of

registered yellow fever vaccination centres in other countries were obtained from ministries of health

websites, literature, and personal communication with health professionals (see references at Table 4). The numbers of trips abroad (departures) by country in 2013 (N=100) were obtained from the World Bank data repository [18]. Data analyses were carried out in Stata 14 [19].

3. Results

The population weighted mean distance to nearest centre varied from 0.6km in London to 7.1km in Northern Ireland. The national mean distance was 2.4km and the maximum distance 30.9km. Only 1% of the general population had more than 16.1km to their nearest centre (99th percentile) (Table 1, Figure 1, Figure 2).

A total of 713,548 trips to countries with yellow fever transmission risk were made by residents in England, Wales, and Northern Ireland in 2015 (Table 2). Nigeria (20.7%), Brazil (14.8%), and Kenya (13.8%) alone accounted for half of all trips and the ten most commonly visited countries combined accounted for 84.3% of all trips (Table 2).

The number of centres by UK Region varied from 51 in Northern Ireland to 858 in London. The number of centres per population varied from 2.8 per 100,000 population in Northern Ireland to 9.9 per 100,000 population in London. Nationally, there were 5.4 centres per 100,000 population (Table 3).

The size of the centres in terms of the yearly number of vaccines administered was calculated from data submitted in annual surveys in 2013-2015. The average number nationally was 40 vaccines per centre. The London average was the highest at 59 vaccines per centre followed by Northern Ireland (45), South East (40), North West (38), North East (38), East of England (34), South West (34), Yorkshire and The Humber (29), West Midlands (28), Wales (27) and East Midlands (25).

There was a linear relationship between the estimated number of yellow fever vaccines administered and the number of trips to countries with yellow fever risk by UK Region, which indicate that there is balance between supply and demand at the regional level (Figure 3).

The number of centres per 100,000 international trips abroad was 6.1 in England, Wales, and Northern Ireland, which was below that of United States (12.1) and above the rest of World Top20 countries in terms of trips abroad (Table 4).

Table 1 Distance to nearest yellow fever vaccination centre for the general population by UK Region (km).

| Region | Min | Median | Mean | p75 | p99 | Max |
|------------------------|-----|--------|------|------|------|------|
| North East | 0.0 | 2.1 | 3.2 | 3.8 | 20.2 | 28.3 |
| North West | 0.0 | 1.6 | 2.0 | 2.7 | 8.7 | 25.0 |
| Yorkshire & The Humber | 0.0 | 1.7 | 2.4 | 3.3 | 10.6 | 26.4 |
| East Midlands | 0.0 | 1.7 | 2.7 | 3.5 | 15.9 | 21.9 |
| West Midlands | 0.0 | 1.5 | 2.1 | 2.5 | 11.5 | 17.3 |
| East of England | 0.0 | 1.5 | 2.8 | 3.6 | 14.6 | 20.9 |
| London | 0.0 | 0.5 | 0.6 | 0.8 | 2.2 | 4.0 |
| South East | 0.0 | 1.2 | 1.9 | 2.4 | 9.6 | 18.7 |
| South West | 0.0 | 1.5 | 2.7 | 3.7 | 14.3 | 23.7 |
| Northern Ireland | 0.0 | 3.9 | 7.1 | 11.9 | 26.4 | 30.9 |
| Wales | 0.0 | 3.2 | 4.9 | 7.5 | 22.0 | 29.3 |
| Total | 0.0 | 1.3 | 2.4 | 2.9 | 16.1 | 30.9 |

Note: The national 56th percentile was 1.6km. The headers, p75 and p99, denote the 75th and 99th percentile, respectively.

Table 2 Top10 Trips abroad to countries with yellow fever risk made by residents in England, Wales, and Northern Ireland. Source: International Passenger Survey 2015.

| Destination | Freq. | Percent | Cumulative Percent |
|-------------------|---------|---------|--------------------|
| Nigeria | 147,856 | 20.7 | 20.7 |
| Brazil | 105,331 | 14.8 | 35.5 |
| Kenya | 98,392 | 13.8 | 49.3 |
| Ghana | 66,558 | 9.3 | 58.6 |
| Gambia | 42,329 | 5.9 | 64.5 |
| Trinidad & Tobago | 37,589 | 5.3 | 69.8 |
| Uganda | 31,814 | 4.5 | 74.3 |
| Argentina | 31,188 | 4.4 | 78.6 |
| Colombia | 22,764 | 3.2 | 81.8 |
| Peru | 17,785 | 2.5 | 84.3 |
| Other | 111,942 | 15.7 | 100.0 |
| Total | 713,548 | 100.0 | - |

Table 3 Trips abroad by Region of residence in England, Wales, and Northern Ireland in 2015 compared to the number of yellow fever vaccination (YFV) centres. YF Trips: trips to countries with yellow fever risk. Trips data source: International Passenger Survey 2015.

| Region | Trips Abroad | YF Trips | YFV Centres | Mean Distance to YFV Centre (km) | Centres per 100,000 Pop | Trips per 100,000 Pop | YF Trips per 100,000 Pop |
|------------------------|--------------|----------|-------------|----------------------------------|-------------------------|-----------------------|--------------------------|
| London | 14,596,697 | 350,422 | 858 | 0.6 | 9.9 | 168,287 | 4,040 |
| South East | 10,338,088 | 114,840 | 572 | 1.9 | 6.4 | 115,536 | 1,283 |
| West Midlands | 4,806,320 | 51,938 | 239 | 2.1 | 4.2 | 83,574 | 903 |
| East of England | 5,777,899 | 50,538 | 324 | 2.8 | 5.3 | 95,087 | 832 |
| North West | 6,568,124 | 39,169 | 251 | 2.0 | 3.5 | 91,557 | 546 |
| South West | 4,629,680 | 35,501 | 299 | 2.7 | 5.5 | 84,619 | 649 |
| East Midlands | 3,774,532 | 25,869 | 211 | 2.7 | 4.5 | 80,703 | 553 |
| Yorkshire & The Humber | 4,752,930 | 23,817 | 208 | 2.4 | 3.9 | 88,171 | 442 |
| North East | 1,844,388 | 16,185 | 85 | 3.2 | 3.2 | 70,273 | 617 |
| Wales | 2,183,671 | 5,267 | 110 | 4.9 | 3.5 | 70,462 | 170 |
| Northern Ireland | 803,150 | 0 | 51 | 7.1 | 2.8 | 43,376 | - |
| Total | 60,075,479 | 713,546 | 3,208 | 2.4 | 5.4 | 100,567 | 1,194 |

Table 4 Yellow fever vaccination centres per international trips abroad by country.

| Rank | Country | Trips abroad (millions) | Yellow fever vaccination centres (YFVC) | YFVC per 100,000 trips abroad |
|------|----------------------------|-------------------------|---|-------------------------------|
| 1 | China [20] | 98.2 | 168 | 0.2 |
| 2 | Germany [21] | 87.5 | 2,072 | 2.4 |
| 3 | Hong Kong SAR, China [22] | 84.4 | 2 | <0.1 |
| 4 | United States [23] | 61.9 | 7,493 | 12.1 |
| 5 | Russian Federation [24] | 54.1 | 44 | 0.1 |
| 6 | England, Wales, N. Ireland | 53.0 | 3,208 | 6.1 |
| 7 | Poland* | 52.6 | . | . |
| 8 | Canada [25] | 33.0 | 1,050 | 3.2 |
| 9 | Italy [26] | 27.8 | 330 | 1.2 |
| 10 | France [27] | 26.2 | 162 | 0.6 |
| 11 | Ukraine* | 23.8 | . | . |
| 12 | Saudi Arabia [28] | 19.2 | 435 | 2.3 |
| 13 | Netherlands [29] | 18.1 | 968 | 5.3 |
| 14 | Japan [30] | 17.5 | 22 | 0.1 |
| 15 | India [31] | 16.6 | 34 | 0.2 |
| 16 | Hungary [32] | 16.0 | 30 | 0.2 |
| 17 | Sweden** | 15.9 | . | . |
| 18 | Mexico [33] | 15.9 | 6 | <0.1 |
| 19 | Korea, Rep. [34] | 14.8 | 23 | 0.2 |
| 20 | Switzerland [35] | 12.4 | 108 | 0.9 |

*) No data were obtained from Poland and Ukraine. **) The vaccine is in principle available from any vaccination centre including family doctors, hospitals and private travel clinics in Sweden.

4. Discussion

This is the first study to look at the geographical accessibility of yellow fever vaccination centres in England, Wales, and Northern Ireland. For comparison, recent studies of geographical accessibility to GP practices and pharmacies found that 84.8% of the general population in England and Wales lived within 1.6km of a GP practice [36]; for pharmacies it was 89.2% [37]. In the present study, only 56% of the population lived within 1.6km of a yellow fever vaccination centre. For comparison, the number of active GP practices in England and Wales in August 2016 was 11,456 [38] and the number of pharmacies, 13,104 [39], whereas only 3,157 yellow fever vaccination centres were registered in England and Wales in October 2016. Only 1% of the population lived more than 16.1km away from a yellow fever vaccination centre. So, while the geographical accessibility of yellow fever vaccination centres is poorer than for general medical services, it does not seem unreasonable taking into account that long-haul trips to countries with yellow fever risk are likely to be planned and are, typically, private undertakings [40].

There was a linear relationship between the estimated number of yellow fever vaccines administered and the number of trips to countries with yellow fever risk by UK Region, which indicate that there is balance between

supply and demand and hence an even service availability at the regional level. No under-served regions were –
 1 in other words – identified.

2
 3
 4 The number of centres per 100,000 international trips abroad was 6.1 in England, Wales, and Northern Ireland,
 5
 6 which was below that of United States (12.1) and above the rest of World Top20 countries in terms of trips
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 8 abroad (Table 4). The reasons for the large variation internationally are likely to be different travel
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 10 patterns/demand and differences in healthcare system.

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 14 The detailed data of the accessibility of yellow fever vaccination centres, will allow the regulator to make
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 16 contingency plans for future vaccine shortages to ensure that vaccination services can be accessed across all
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 18 regions. It will, as an example, be possible to run various scenarios to see the impact on regional accessibility if
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 20 the number of active centres were to drop during a shortage.

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 24 There are a few limitations with using the International Passenger Survey (IPS) data to estimate the regional
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 26 demand of yellow fever vaccinations. First, the IPS does not record all trips on cruise ships (not at all if
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 28 embarkation was in the UK) and the trip may simply be recorded as ‘cruising’ as a generic, multi-country
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 30 destination. In 2015, UK residents undertook an estimated 1.78 million cruise trips (7.7% of global figures)
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 32 [41]. More detailed UK data were not available to estimate the number of trips that would have required yellow
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 34 fever vaccination either due to exposure risk or itinerary-based vaccination certificate requirements. Data on
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 36 the cruise tourism industry as a whole in 2011, however, suggest that only a small fraction of cruise trips is
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 38 likely to require yellow fever vaccination [42]. The Caribbean and the Mediterranean account for more than
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 40 70% of bed-days. Within the Caribbean most itineraries cover the ports in the United States, Bahamas, Eastern
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 42 and Western Caribbean and the South American ports are much less visited. Most cruises only take seven days
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 44 and use hub ports such as Miami, Fort Lauderdale, or San Juan, Puerto Rico, in the northern half of the
 45
 46 Caribbean. South America accounts for 5.4% of the global number of bed-days and the majority of visits are to
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 48 certain coastal regions outside the yellow fever risk areas. Future studies of actual itineraries (including inland
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 50 trips and excursions) may be able to more realistically highlight any discrepancies between risk and protection,
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 52 e.g. in South America and Eastern Panama [43]. Second, the data for yellow fever risk are provided by WHO at
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 54 the country-level, whereas in practice it will for countries only partly endemic depend on a risk assessment of
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 56 the individual traveller including regions to be visited within a country (which may change during large
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 58 outbreaks), duration, and planned activities. Examples of countries that are only partly endemic are Brazil,
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Peru, and Kenya. Third, if a traveller plan to visit more than one country, the IPS record relate to the country where the traveller spend the most time. A travel itinerary where a yellow fever risk country is only a secondary destination would therefore not be counted. Fourth, the IPS only cover about 0.2% of all trips abroad [1] and rarely visited destinations may not be detected.

5. Conclusion

The geographical accessibility of yellow fever vaccination centres was good across all major population centres considering that that long-haul trips to countries with yellow fever risk are likely to be planned. Vaccines administered was found correlated with the number of trips to yellow fever countries at regional level in England, Wales, and Northern Ireland, which indicate an even service availability. A large variation was found between countries in the number of yellow fever vaccination centres per trips abroad. England, Wales, and Northern Ireland were together with United States and the Netherlands among the countries with the most yellow fever vaccination centres per trips abroad. The reasons for the large variation internationally are likely to be different travel patterns/demand and differences in healthcare system.

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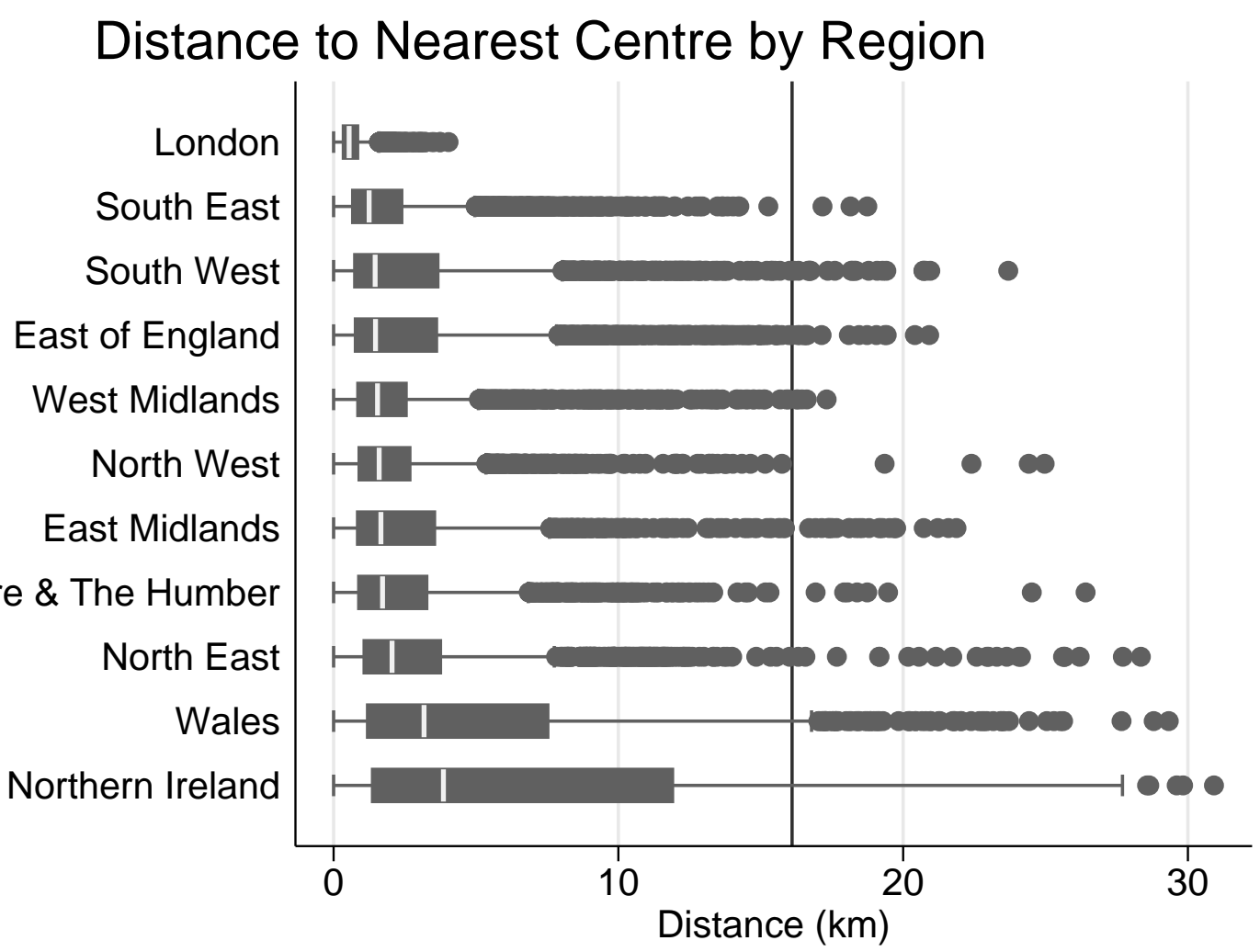
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FIGURE LEGENDS

Figure 1 Distance to nearest yellow fever vaccination centre for the general population by UK Region (km).

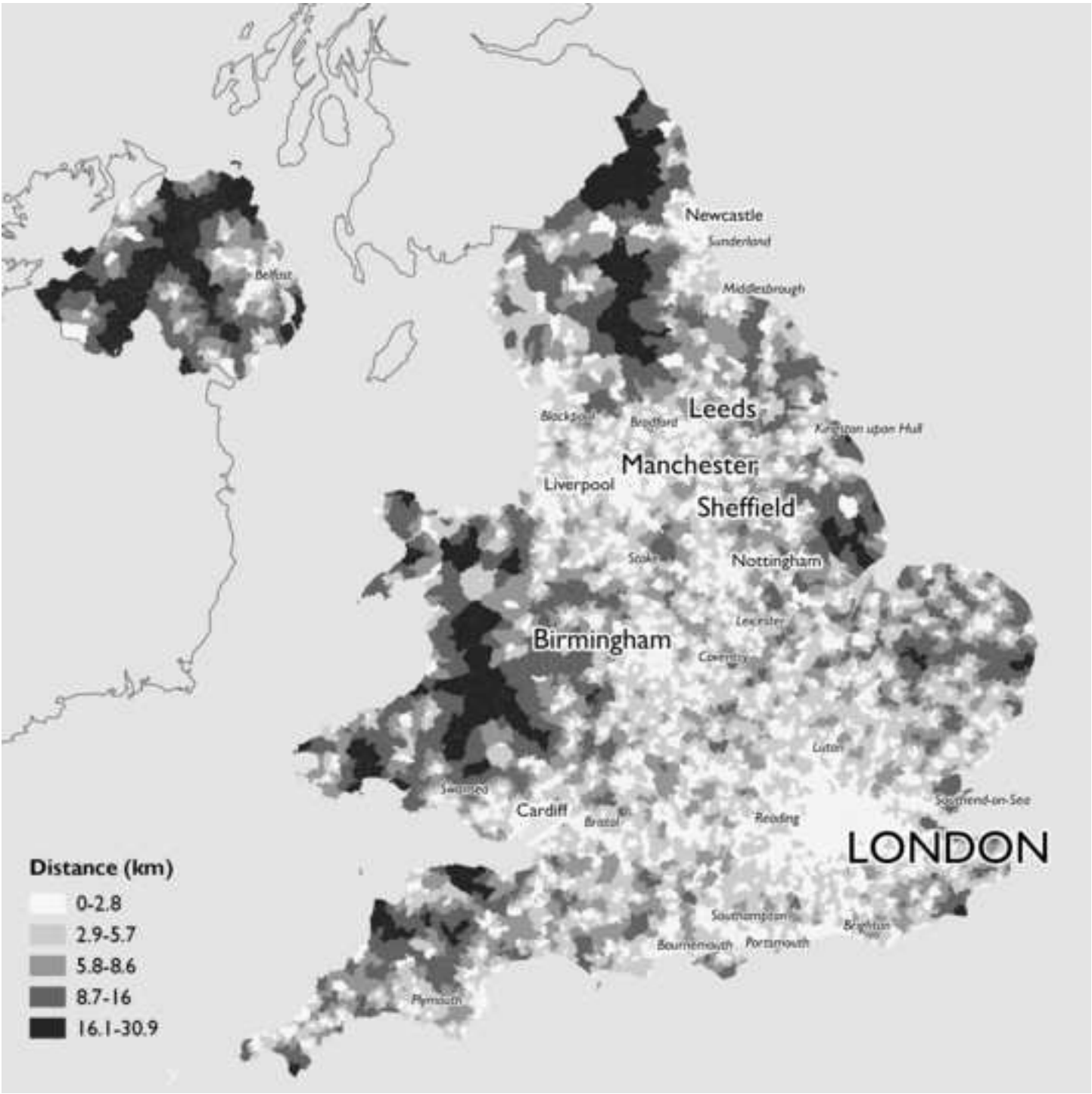
Figure 2 Distance (km) to nearest yellow fever vaccination centre in England, Wales, and Northern Ireland (lower layer super output area level).

Figure 3 Estimated number of yellow fever vaccinations and trips to countries with yellow fever risk by region of residence in England, Wales, and Northern Ireland. Labels: North East (NE), North West (NW), Yorkshire & The Humber (YH), East Midlands (EM), West Midlands (WM), East of England (EE), London (LO), South East (SE), South West (SW), Wales (WA), Northern Ireland (NI).



Figure

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Figure

